REMARKS/ARGUMENTS

Status of the claims

Claims 21-22, 24, 86-89 and 99-100 are pending and examined on the merits. Claims 1-20, 23, 25-85 and 90-98 are withdrawn. Claim 21 has been amended to recite that the zinc finger protein is engineered as described at e.g., paragraph 188 of the published application. Engineering means that the sequence of a natural zinc finger protein is changed by rational design or randomization/selection to confer a desired binding specificity (see paragraphs 188-199 and 215 of published application). Entry of the amendment is respectfully requested because it is explicitly supported by the specification and either puts the claims in condition for allowance or simplifies issues for appeal.

Information Disclosure Statement

Applicants note that, on the March 25, IDS, citation AA was not initialed by the Examiner. Applicants request confirmation that this reference has been considered, and the provision of an initialed SB/08A to that effect.

Election/Restrictions

The Examiner acknowledges that independent claim 21 can be searched without the need of a particular sequence. Office Action, paragraph 2. However, claim 23 remains withdrawn on the basis that claims 21-22 have been examined to the extent that the nucleic acid sequences consists of three zinc fingers. In response, it is respectfully submitted that claims 21 and 22 should have been examined across their full scope. Claim 22 refers to zinc finger proteins that comprise three fingers, not that consist of three fingers. Claim 21 must be at least as broad as claim 22 in this respect. Because both of these claims can be searched without reference to any particular sequence, there is no basis to confine the search to zinc finger proteins consisting of three zinc fingers. Likewise, if claims 21 and 22 are searched across their full scope, there is no reason not to examine claim 23 as well.

35 U.S.C. § 102

Applicants use the paragraph numbering of the office action in responding to the rejections.

6. Claims 21, 22, 24 and 100 stand rejected under 35 U.S.C. § 102(b) as anticipated by Sif. Sif is said to teach a purified cDNA molecule encoding the transcription factor Sp1. Ryuto is cited as providing knowledge in the art that Sp1 binds to the VEGF gene. Berg is cited as disclosing that Sp1 consists of three zinc finger domains. Sif is also alleged to teach a fusion of SP1 with a GST domain in which the GST domain regulates the binding of Sp1 to glutathione. Sif is also said to disclose a vector that comprise a nucleic acid encoding a Sp1 protein (citing to p. 7132). This rejection is respectfully traversed.

Sif discusses the natural transcription factor Sp1 and a derivative thereof in which the transactivation domain of Sp1 is fused to a GAL4 DNA-binding domain. *See* Sif at page 7132, second column, first paragraph of "Results" section, which states that the GAL4/Sp1 fusion protein ". . . lack[s] the C-terminal DNA-binding domain [of Sp1]." Sif also discusses a GST/Sp1 fusion protein containing the same portion of Sp1 (amino acids 83-621) (see p. 7132, first column, first paragraph). Thus, the Sp1/GST fusion also lacks the DNA-binding domain of Sp1.

The natural Sp1 protein discussed by Sif is not an engineered zinc finger protein, as specified in the amended claims. Because Sif's Sp1/GAL4 fusion protein lacks the Sp1 DNA-binding domain, there is no reason to expect that it would bind to any Sp1 binding site, let alone an Sp1 binding site present in a VEGF gene. Sif's Sp1/GAL4 fusion protein would thus not be expected to bind to a VEGF gene, much less regulate angiogenesis. Similarly, Sif's GST/Sp1 fusion protein contains the same portion of Sp1 (amino acids 83-621) that is present in the GAL4/Sp1 fusion. *See* Sif at page 7133, first column, second paragraph. Therefore, the GSP/Sp1 fusion also lacks the DNA-binding domain of Sp1 and is incapable of binding to an Sp1 binding site in a VEGF gene or any other gene. Accordingly, neither the natural Sp1 protein nor the two fusion proteins incorporating part of Sp1 discussed by Sif meet the claim

requirement of an engineered zinc finger protein that binds to a target site in a VEGF gene so as to modulate expression of the VEGF gene, thereby modulating angiogenesis.

For these reasons, withdrawal of the rejection is respectfully requested.

8. Claims 21, 22, 24, 86-89 and 100 are rejected under 35 USC 102(e) as anticipated by Case, US 6,599,692. Case is said to disclose a nucleic acid that encodes a zinc finger protein in which the zinc finger protein has at least three fingers and is capable of targeting a VEGF gene. Case is also said to disclose that the nucleic acid encoding the zinc finger protein can be part of a chimeric protein in which the zinc finger protein is linked to a regulatory domain. Case is also said to disclose that a zinc finger protein can be used for in vivo purposes and the use of viral expression vectors. This rejection is respectfully traversed.

Case reports that two zinc finger proteins were able to activate and inhibit an endogenous VEGF gene in cell culture (see cols. 41-42). However, Case does not disclose any experiments to test whether the zinc finger proteins could modulate angiogenesis. Angiogenesis is a complex process involving many molecules besides VEGF. It was not known whether either of the two zinc finger proteins, reported by Case to regulate VEGF in cell culture, necessarily modulated angiogenesis. As noted above, inherent anticipation may not be established by probabilities or possibilities. Further, the examiner bears the burden of establishing a prima facie case of anticipation based upon the prior art (*In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984)). Here, absent a showing that either of the zinc finger proteins disclosed by Case necessarily modulates angiogenesis, it is respectfully submitted that the Examiner has not fulfilled the burden of proof required for anticipation.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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